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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,451	10/04/2005	Frank Giles	ON/4-32719A	3037

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
KUDLA, JOSEPH S	

ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,451	GILES, FRANK	
	Examiner	Art Unit	
	JOSEPH S. KUDLA	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *6-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Foreword

1. Applicants' Amendment-After Non-Final Rejection and receipt of two foreign patent application references, filed April 17, 2008, are acknowledged. With respect to Applicants' Arguments/Remarks in the correspondence, the arguments and request for reconsideration have been fully considered and are found not persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejection and objection are newly applied. They constitute the complete set presently applied to the instant specification.

Claims 1-5 are presented for examination on the merits as they read upon the elected subject matter.

Information Disclosure Statement

2. The information disclosure statement correspondences submitted by Applicant on May 17, 2006 are acknowledged. The references have been reviewed to the extent each is a proper citation on a U.S. Patent.

Claim Rejections - 35 USC § 103

(Original Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wood et al. (cited in previous office action), further in view of Barosi et al. (cited in previous office action).

Tille teaches that PTK787 is an effective inhibitor of b-FGF (Abstract: 1073, Results: page 1076).

Tille does not teach that PTK787 may be used to treat AMM.

Barosi teaches that deregulation of the b-FGF pathway in primitive hematopoietic stem cells is hypothesized to be a primary event in the abnormal hematopoiesis of MMM (also known as AMM) (page 2955, Myeloid Proliferative Advantage, col. 2, paragraph 2). It would have been reasonable to expect that inhibition of this pathway would be a treatment for AMM.

Since Tille teaches PTK787 inhibits the b-FGF pathway, and Barosi suggests b-FGF pathway inhibition would likely be a treatment for AMM, it would have been obvious for some one of ordinary skill in the art to administer PTK787 as a b-FGF

inhibitor to treat AMM.

Tille et al. teach vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) are potent angiogenic inducers (Abstract, first sentence). Tille et al. teach vascular endothelial growth factor receptor-2 (VEGFR-2) antagonist, such as PTK-787, can inhibit mediators of angiogenesis (i.e., VEGF and bFGF) (Abstract, last sentence and page 1074, under Materials and Methods, under Reagents, first sentence). Tille et al. teach that human umbilical vein endothelial (HUVE) cell proliferation could be achieved by inhibition of the bFGF pathway or VEGF pathway with the administration of PTK-787, although concentrations of PTK-787 required to inhibit bFGF induced proliferation were 100 to 1000-times higher than for the concentrations of PTK-787 required to inhibit VEGF-induced proliferation (page 1076, column 2, paragraph 2). Tille et al. teach inhibition of angiogenesis with PTK-787 in an *in vivo* model of angiogenesis through either the VEGF or bFGF pathways (page 1077, column 1, paragraph 2 and page 1079, Figure 4).

Tille et al. does not teach PTK-787 can treat agnogenic myeloid metaplasia (AMM).

Barosi teaches that “at a cellular level, the proliferative advantage of the mutated clone is documented by the elevated *in vitro* growth of hematopoietic progenitor cells, by their enhanced sensitivity to hematopoietic growth factors" (page 2955, column 1, under Myeloid Proliferative Advantage, sentence 2). Barosi teaches this clonal proliferative event is primary to all chronic myeloproliferative disorders, however, is

specific to AMM in "that it subsequently produces an abnormal population of hematopoietic cells that inappropriately release fibrogenic cytokines and/or growth factors in the bone marrow" which eventually serve to colonize extramedullary sites (page 2954, column 1, paragraph 1). Barosi teaches "this functional derangement of the hematopoietic cell clone" results in "progressive splenomegaly caused by myeloid metaplasia" (page 2954, column 2, paragraph 1). Barosi teaches that "deregulation of the bFGF pathway in primitive hematopoietic stem cells is hypothesized to be a primary event in the abnormal hematopoiesis of AMM (page 2955, column 2, paragraph 2).

It would have been obvious to one of ordinary skill in the art at the time of the invention that if one had an agent that could inhibit the bFGF pathway, one could effectively halt the colonization of extramedullary sites and thus prevent the extramedullary hematopoiesis that usually results in splenomegaly and occasionally accompanied by hepatomegaly in later stages of the disease. Therefore, if one possessed such an agent, one would be able to treat a clinical sign of AMM. It would have been obvious to one of ordinary skill in the art at the time of the invention that since Tille et al. teach that PTK-787 functions as an inhibitor of bFGF, one of ordinary skill in the art would have the expectation that PTK-787 would be an effective treatment for AMM, therefore rendering instant claims 1-3 obvious. It would have been obvious to one of ordinary skill in the art that since Tille et al. teach that PTK-787 is effective at inhibiting the bFGF pathway in an *in vivo* model of angiogenesis (thus representing an art accepted method of treating a mammal such as a human) claim 5 is rendered obvious. It would have been obvious to one of ordinary skill in the art that, regardless of

whether the disease is resistant to conventional therapy, the administration of PTK-787 to a mammal would have the expectation of reducing the colonization of extramedullary sites, thus prevent the extramedullary hematopoiesis that usually results in splenomegaly effectively treating AMM, therefore rendering instant claim 4 obvious.

Applicant's arguments have been fully considered but found not to be persuasive.

A. Applicant's argument that the reference discloses that all compounds tested are inactive against bFGF-induced proliferation at the at the concentration range required for VEGFR inhibition making it not clear to Applicant that Tille et al. makes a teaching attributed to it by the Examiner.

See Tille et al. citations *supra*. Tille et al. teach that human umbilical vein endothelial (HUVE) cell proliferation could be achieved by inhibition of the bFGF pathway or VEGF pathway with the administration of PTK-787, although concentrations of PTK-787 required to inhibit bFGF induced proliferation were 100 to 1000-times higher than for the concentrations of PTK-787 required to inhibit VEGF-induced proliferation (page 1076, column 2, paragraph 2). In addition, Figures 2 and 4 of Tille et al. clearly demonstrate that PTK-787 inhibits the bFGF pathway.

B. Applicant requests the Examiner to identify the sections of the reference which are relied upon for the teaching attributed to it.

See the expounded ***35 USC § 103 Claim Rejection*** *supra*.

C. Applicant's argument that the Barosi reference does not provide a basis for the skilled artisan to have a reasonable expectation that an inhibitor of b-FGF would be useful to treat AMM.

Applicant is reminded of M.P.E.P. § 2123. "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)).

A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including non-preferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also > Upsher-Smith Labs. v. Pamlab, LLC, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005)(reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component);< Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed.").

One of ordinary skill in the art at the time of the invention would expect that because it was *explicitly* disclosed in the Barosi reference that "deregulation of the bFGF pathway in primitive hematopoietic stem cells is hypothesized to be a primary event in the abnormal hematopoiesis of AMM (page 2955, column 2, paragraph 2), that if one possessed an inhibitor the bFGF pathway, one could effectively treat AMM.

No claim is allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph S. Kudla whose telephone number is (571) 270-3288. The examiner can normally be reached on 9am - 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph S. Kudla/
Examiner Art Unit 1611
July 16, 2008

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615